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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/699,027	10/27/2000	Jonathan L. Sessler	4201.01 US	6781

32270 7590 09/12/2003

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EXAMINER

LUKTON, DAVID

ART UNIT	PAPER NUMBER
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1653

DATE MAILED: 09/12/2003

14

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/699,027

Applicant(s)

SESSLER ET AL.

Examiner

David Lukton

Art Unit

1653

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 08 July 2003.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-27 is/are pending in the application.
- 4a) Of the above claim(s) 1-19,22,23 and 25-27 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 20 and 21 is/are rejected.
- 7) ☒ Claim(s) 24 is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____.
- 4) ☐ Interview Summary (PTO-413) Paper No(s). _____.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: _____.

Pursuant to the response filed 7/8/03, no claim has been added, amended, or deleted.

Claims 1-27 remain pending. Claims 20, 21, 24 are examined in this Office action; claims 1-19 and 25-27 remain withdrawn from consideration. In addition, claims 22-23 are withdrawn from consideration, since they do not encompass the elected species.

Applicants' arguments filed 7/8/03 have been considered and found not persuasive.

✱

The following is a quotation of 35 USC §103 which forms the basis for all obviousness rejections set forth in the Office action:

A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Subject matter developed by another person, which qualifies as prior art only under subsection (f) and (g) of section 102 of this title, shall not preclude patentability under this section where the subject matter and the claimed invention were, at the time the invention was made, owned by the same person or subject to an obligation of assignment to the same person.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103, the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made, absent any evidence to the contrary. Applicant is advised of the obligation under 37 C.F.R. 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103.

Claim 20 is rejected under 35 U.S.C. §103 as being unpatentable over Sessler (USP 5,622,946) in view of Lehninger (Biochemistry, 2nd Edition, pages 641-642; Worth

Publishers, 1975).

As indicated previously, Sessler discloses a method of inducing oxidative stress by administering a compound that meets the requirements of instant claim 20, step (a).

Lehninger discloses that oxygen and water are both "precursors" of ascorbate.

In response to the foregoing, applicants have argued that claim 20 differs from the prior art in that claim 20 does not require ionizing radiation. However, claim 20 does permit ionizing radiation, and so claim 20 is not distinguished on this basis.

Applicants have also argued that the question of biosynthesis of ascorbic acid is irrelevant to the claimed invention. However, applicants are not correct on this point. Claim 20, step (c) recites the step of administering a precursor of a cellular metabolite. The preferred "cellular metabolite" is ascorbic acid, as is evident from a reading of claim 21, and as evident also from a reading of page 18, lines 18-22 of the ^{specification} ~~specification~~. Thus, any precursor of ascorbic acid would be included. Given that any precursor of ascorbic acid is included in step (c), the biosynthesis of ascorbic acid is an issue that is directly relevant to the claimed invention.

The rejection is maintained.

✱

Claim 20 is rejected under 35 U.S.C. §103 as being unpatentable over Sessler (USP 5,622,946) in view of Lehninger (Biochemistry, 2nd Edition, pages 503-504; Worth Publishers, 1975).

As indicated previously, Sessler discloses a method of inducing oxidative stress by administering a compound that meets the requirements of instant claim 20, step (a). Sessler does not explicitly disclose that the patient should be allowed to breathe air, nor does Sessler disclose that molecular oxygen is a cellular metabolite.

Lehninger discloses that molecular oxygen is a cellular metabolite; it is produced, for example, by superoxide dismutase, and by catalase. Lehninger does not disclose a method for inducing targeted oxidative stress.

The first point to be made is that the "cellular metabolite" of step (c) is met by simply letting a patient breathe air. The oxygen that is present in air is not produced primarily by SOD or catalase. Rather, it is produced by plants. Thus, oxygen is a "cellular metabolite" wherein the cells are those present in plants. The fact that oxygen is a "cellular metabolite" is actually a sufficient basis for this rejection (in conjunction with the teachings of Sessler). But independently of that fact, Lehninger discloses that molecular oxygen is a "cellular metabolite" in mammalian systems. Thus, any person who breathes air is administering to himself (or herself) a "cellular metabolite", either that of an animal or of a plant.

The second point is that molecular oxygen begets reactive oxygen species. Thus, a person who is breathing air will produce reactive oxygen species. Accordingly, the limitations of step (c) are met merely by simply breathing air.

Thus, the claim is rendered obvious.

*

Claims 20 and 21 are rejected under 35 U.S.C. §103 as being unpatentable over Vogel (USP 5,244,671).

Vogel disclose the use of photactivatable porphycenes. Also disclosed (e.g., col 6, line 66) is the production of singlet oxygen following irradiation. Also disclosed (col 7, line 32) is the co-administration of ascorbic acid.

In response to the foregoing, applicants have argued that the intended use of the ascorbic acid in Vogel is inhibition of oxidation, rather than promotion of oxidation. The first point is that nowhere in Vogel is there any suggestion that ascorbic acid will fail to promote production of reactive oxygen species *in vivo*. Vogel, in fact, is silent on this matter. But the reference does affirmatively teach administration of a porphycene in combination with ascorbic acid. Applicants have argued that because Vogel has characterized ascorbic acid as an anti-oxidant, ascorbic acid will therefore fail to promote oxidation *in vivo*. However, the behavior and reactivity of molecules is not determined by the assertions or wishes of persons observing them. Instead, the the behavior and reactivity of molecules is determined by the reaction conditions, and by the laws of chemistry and physics. If Vogel had explicitly stated that he very much “hopes” that ascorbic acid will not promote production of reactive oxygen species *in vivo*, that would not change the outcome. The molecules are not aware of what people think about them. However, if applicants have evidence that ascorbic acid will fail to promote production of reactive oxygen species *in*

vivo, applicants are invited to present such.

In addition to the foregoing, there is actually no conflict between stating, on the one hand, that ascorbic acid is a reducing agent, and at the same time, that ascorbic acid can facilitate the conversion of molecular oxygen to superoxide or hydrogen peroxide, or hydroxyl radical.

If ascorbic acid transfers an electron to molecular oxygen through the intermediacy of a transition metal ion (e.g., copper or iron), the result will be that ascorbic acid has fulfilled its role of a reductant, but at the same time, superoxide will be generated.

The rejection is maintained.

*

Claims 20 and 21 are rejected under 35 U.S.C. §103 as being unpatentable over Vogel (USP 5,244,671) in view of Kimoto (*Cancer Research* **43** (2) 824-8, 1983) or Bram (*Nature* 284 (5757) 629-31, 1980).

The teachings of Vogel were indicated previously. Vogel does not disclose that ascorbic acid will enhance the anticancer activity of the Vogel compounds. Kimoto and Bram disclose that ascorbic acid is an anticancer agent in the presence of oxygen. Thus, the practitioner of the Vogel invention would recognize that the ascorbic acid will produce additive effects in the treatment of cancer.

The claims are rendered obvious.

*

Claims 20 and 21 are rejected under 35 U.S.C. §103 as being unpatentable over Platzek

(USP 6,136,841).

Platzek discloses the use of porphyrins for photodynamic therapy. Also disclosed (col 7, line 57) is the co-administration of the porphyrin with ascorbic acid.

Applicants have traversed this ground of rejection for the same reason as given in the traversal of the rejection over Vogel. Applicants have argued that (a) the behavior of molecules is determined by the wishes of observers, rather than by the laws of chemistry and physics, and (b) that if a compound is a reductant, it cannot transfer a single electron to molecular oxygen, thereby generating reactive oxygen species. Applicants are incorrect on both of these points, as discussed above in the rejection over Vogel.

The rejection is maintained.

*

Claims 20 and 21 are rejected under 35 U.S.C. §103 as being unpatentable over Platzek (USP 6,136,841) in view of Kimoto (*Cancer Research* **43** (2) 824-8, 1983) or Bram (*Nature* 284 (5757) 629-31, 1980).

The teachings of Platzek were indicated previously. Platzek does not disclose that ascorbic acid will enhance the anticancer activity of the Platzek compounds. Kimoto and Bram disclose that ascorbic acid is an anticancer agent in the presence of oxygen. Thus, the practitioner of the Platzek invention would recognize that the ascorbic acid will produce additive effects in the treatment of cancer.

The claims are rendered obvious.

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No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David Lukton whose telephone number is 703-308-3213. The examiner can normally be reached Monday-Friday from 9:30 to 6:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christopher Low, can be reached at (703) 308-2923. The fax number for the organization where this application or proceeding is assigned is 703-872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.



DAVID LUKTON
PATENT EXAMINER
GROUP 1000